## DT04 Rec'd PCT/PT0 2 2 SEP 2004

## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

- 1. (Original): A process for preparing a humanized antibody comprising the steps of: (a) selecting a specificity determining residue (SDR) of the complementarity determining region (CDR) of murine monoclonal antibody heavy chain and light chain variable regions; and (b) grafting said SDR to at least one of the corresponding amino acid sequences into human antibody variable regions.
- 2. (Original): The process of claim 1, wherein step (a) is conducted by replacing each the amino acid residues of CDR with alanine to produce transformants, selecting a transformant that has lower affinity to the human antigen (K<sub>D</sub>) than the original murine antibody and determining the replaced 15 amino acid residue of said transformant as an SDR.
- 3. (Currently amended): The process of claim 2, wherein the CDR is selected from the group consisting of HCDR1(aa 31-35), HCDR2(aa 50-65) and HCDR3(aa 95-102) of the heavy chain (SEQ ID NO: 2); and LCDR1(aa 24-34), LCDR2(aa 50-56) and LCDR3(aa 89-97) of the light chain (SEQ ID NO: 4) of the murine monoclonal antibody variable regions of hepatitis B virus pre-S1 antigen, selecting a transformant that has an affininty affinity to antigen which is more than 3 times lower than the original murine antibody when replaced with alanine,

DE-1586 -3-

determining the replaced amino acid residue of said transformant as an SDR, and grafting said SDR to the corresponding amino acid sequence in human antibody heavy chain and light chain.

- 4. (Original): The process of claim 3, which is characterized in that the at least one of Trp33, Met34, and Asn35 of HCDRI; Arg50, Tyr52, and Pro52a of HCDR2; and G1u95, Tyr96, and G1u98 of HCDR3 of the murine monoclonal antibody KR127 heavy chain, is grafted to the corresponding amino acid sequences in human antibody heavy chain.
- 5. (Original): The process of claim 4, which is characterized in that the at least one of the following grafting steps is carried out:
  - (a) the amino acid residue at position 32 in HCDR1 of human antibody with alanine;
  - (b) the amino acid residue at position 97 in HCDR3 of human antibody with arginine or alanine;
  - (c) the amino acid residue at position 98 in HCDR3 of human 5 antibody with valine; and
  - (d) the amino acid residue at position 102 in HCDR3 of human antibody with arginine or alanine.
- 6. (Original): The process of claim 5, which is characterized in that the at least one of Trp33 and Asn35 of HCDRI; Arg50 and Tyr52 of HCDR2; and Arg95 and Tyr96 of HCDR3 of the murine monoclonal antibody KR1 27 heavy chain, is grafted into the human antibody heavy chain DP7-JH4.

· DE-1586 -4-

- 7. (Currently amended): The process of claim 6, which is characterized in that the amino acid residues of the Ala71 and Lys73 in Framework region 3 of the murine monoclonal antibody KR127 heavy chain variable region, of are further grafted into the human antibody heavy chain DP7-JH4.
- 8. (Original): The process of claim 3, which is characterized in that the at least one of the Leu27b, Tyr27d, Ser27e, Asn28, Lys30, Tyr32 and Asn34 of LCDR1; Leu50 and Asp55 of LCDR2; and Val89, Gln90, Gly9I, Thr92, His93, Phe94, Pro95, and G1n96 of LCDR3 of the murine monoclonal antibody KR1 27 light chain, is grafted into the human antibody light chain.
- 9. (Original): The process of claim 8, which is characterized in that the Tyr27d, Asn28, Asn34 of LCDR1; Leu50 and Asp55 of LCDR2; and Val89, Gly91, Thr92, His93, Phe94, Pro95, and Gln96 of LCDR3 of the murine monoclonal antibody KR127 light chain, is grafted into the human antibody light chain DPH12-JK4.
- 10. (Original): The process of claim 8, which is characterized in that the Leu36 and Arg46 in Framework region 2 of the murine monoclonal antibody KR127 light chain variable region, are further grafted into the human antibody light chain DPH12-JK4.

· DE-1586 -5-

- 11. (Original): A humanized antibody prepared by the process of any one of claims 1 to 10, which has an affinity to antigen of higher than 8.2 x 1 0<sup>9</sup> M and suppresses HAMA (human anti-mouse antibody) response to a greater extent than an antibody prepared according to CDR-grafting method.
- 12. (Original): The humanized antibody of claim 11, which has the amino acid sequence of SEQ ID NO: 2 for the heavy chain variable region of HBV pre-S1 antigen.
- 13. (Original): The humanized antibody of claim 11, which has the amino acid sequence of SEQ ID NO: 4 for the light chain variable region of HBV pre-S1 antigen.
- 14. (Currently amended): The A humanized antibody of any one of claims 11 to 13, which is produced by CHO/HuKR127 (Accession No.: KCTC 10199BP).
- 15. (Original): A DNA encoding the humanized antibody heavy chain containing the amino acid sequence of SEQ ID NO: 2 for the heavy chain variable region of HBV pre-S1 antigen.
- 16. (Original): The DNA of claim 15, wherein the variable region has the nucleotide sequence of SEQ ID NO: 1.

DE-1586 -6-

17. (Original): A DNA encoding the humanized antibody light chain containing the amino acid sequence of SEQ ID NO: 4 for the light chain variable region of HBV pre-S1 antigen.

- 18. (Original): The DNA of claim 17, wherein the variable region has the nucleotide sequence of SEQ ID NO: 3.
- 19. (Original): An expression vector pHuKR127HC comprising the DNA of claim 16 for expressing the humanized antibody heavy chain for HBV pre-S1 antigen.
- 20. (Original): An expression vector pHuKR127KC comprising the DNA of claim 18 for expressing the humanized antibody light chain for HBV pre-S1 antigen.
- 21. (Currently amended): An expression vector pdCMV-dhfrC-HuKR127 comprising both the DNAs of claim 16 and 18 the nucleotide sequences of SEQ ID NO:1 and SEQ ID NO:3 for expressing the humanized antibody light and heavy chains for HBV pre-S1antigen.
- 22. (Original): An *E. coli* DH5α/pdCMV-dhfrC-HuKR127 (Accession No.: KCTC 10198BP) transformed with the expression vector of claim 21.

DE-1586 -7-

23. (Original): CHO cell line CHOIHuKR127 (Accession No.: KCTC 1010199BP) producing the humanized antibody of claim 11.

24. (Currently amended): A composition for preventing or treating HBV infection comprising the humanized antibody of any one of claims claim11 to 13.